# Correlation between Serum-Ascites Albumin Gradient and Esophageal Varices in Patients with Portal Hypertension

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**Abstract**: Portal hypertension is responsible for complications of cirrhosis such as bleeding esophageal varices (EV) and ascites. The aim of this study is to investigate the correlation between serum-ascites albumin gradient (SAAG) and presence of EV and their grades in patients with portal hypertension. **Patients and Methods:** Thirty three chronic liver disease patients with ascites were studied. They were subjected to clinico-laboratory assessment, ascitic fluid analysis, calculation of SAAG, abdominal ultrasonography and upper gastrointestinal endoscopy. **Results:** The results showed that a cutoff ">1.4" for SAAG to predict the presence of varices with a specificity and a positive predictive value of 100%, the accuracy of this cutoff was 56.1%. However, it had a low sensitivity and a low negative predictive value. A cutoff ">1.2" for SAAG to discriminate between large and small varices yielded a specificity of 69.2% and a positive predictive value of 66.7%, the accuracy of this cutoff was 60%. However, it had a relatively low sensitivity and low negative predictive value. **Conclusions:** A cutoff ">1.4" for SAAG to predict the presence of varices yielded a specificity and a positive predictive value of 100%, the accuracy of this cutoff was 56.1%.

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**Key words:** Portal hypertension, esophageal varices, ascites, serum-ascites albumin gradient.

## Introduction

Portal hypertension is responsible for the more severe and often lethal complications of cirrhosis such as bleeding esophageal varices (EV) and ascites. Almost 35% - 70% of patients with cirrhosis develop EV and approximately 30% of these varices bleed [(1)].

Calculation of the serum-ascites albumin gradient (SAAG) provides useful diagnostic information in patients with ascites [(2)]. This is done by subtracting the ascitic fluid albumin from the serum albumin in simultaneously obtained samples [(3)].

In several studies on cirrhosis due to alcohol, the correlation between SAAG and EV was emphasized and additionally, SAAG was proposed to be a factor determining the degree of portal hypertension and the prognosis of patients with cirrhosis due to alcohol [(4, 5)]. However, this correlation between SAAG and EV could not be found in patients with non-alcoholic cirrhosis [(29)].

In a previous study performed by **Hoef [(4)],** an excellent correlation was found between portal hypertension and SAAG. In patients with ascites, the presence of EV was associated only with high SAAG. In that study, 93% of included patients had alcoholic cirrhosis.

Also, the presence of EV in patients with ascites and high SAAG was directly related to the level of SAAG. However, the size of EV in those patients was not correlated with the level of SAAG [(6)].

## Aim of the work:

This study aims to investigate the correlation between serum-ascites albumin gradient (SAAG) and presence of esophageal varices (EV) and their grades in patients with portal hypertension due to chronic liver disease.

## Patients and Methods

This cross-sectional study was conducted on 33 chronic liver disease patients with ascites due to portal hypertension admitted to Tropical Medicine and Internal Medicine Departments, Ain Shams University Hospital.

**Inclusion criteria:**

- Presence of Chronic liver disease as evidenced by: abdominal Ultrasound and liver profile derangement.
- Presence of portal hypertension as evidenced by: the presence of splenomegaly, portal vein diameter > 13 mm.
- Presence of ascites detected by examination and confirmed by abdominal ultrasound.

**Exclusion criteria:**

- Causes of ascites other than chronic liver disease e.g. congestive heart failure, renal failure or tuberculosis.
- Hepatocellular carcinoma.

**Patients were subjected to:**

**I- Complete history taking.**

**II- Thorough clinical examination.**

**III- Laboratory investigations, including:**

1- Liver profile: including (AST, ALT, S. Albumin, total bilirubin, direct bilirubin, prothrombin time).
2- Complete blood picture (CBC).
3- Renal function Tests: serum blood urea nitrogen (BUN), Creatinine, sodium and potassium levels.
4- Hepatitis markers: hepatitis B surface antigen (HBs Ag) and hepatitis C virus antibody (HCV Ab) by third generation ELISA test.

**IV- Ascitic fluid analysis:** by taking 20 cc of ascitic fluid under complete aseptic condition.

- Physical analysis: including colour, aspect and reaction.
- Chemical analysis: including albumin, total protein, LDH and glucose levels.

Albumin was measured using a diagnostic reagent **(Albumin Fs*)** manufactured by Diasys Diagnostic Systems GmbH (bromocresol purple) for quantitative in vitro determination of albumin in serum or plasma on photometric systems. The measuring range of this reagent is (0.2 – 6 g/dl). The sensitivity (the lower limit of detection) is 0.2 g/dl. Synchron CX9 ALX clinical system, is the machine used for detection of albumin.

- Bacteriological analysis: including: gram stain, Ziel Nielsen stain, leishmann stain, cultures of all the ascitic fluid samples with inoculation for 48 hours and cell count.
- Cytological analysis: including cell type and number.

**V- Calculation of SAAG:** by subtracting the albumin concentration of the ascitic fluid from the albumin concentration of a serum specimen obtained on the same day, (serum albumin – ascitic fluid albumin) [6].

**VI- Patients were classified according to modified Child's classification into:** Child's score A, B and C [7].

**VII- Abdominal Ultrasonography:** Using Toshiba agonistic ultrasound equipment (model SSA-326A).

- ***Liver size***: was classified as Shunken (<11 cm), average (11 – 15), or enlarged (>15 cm) [8].
- ***Liver echogenicity:*** bright or coarse echopattern.
- ***Criteria suggestive of chronic liver disease and cirrhosis*** [9, 10]***:***
  - Increased liver echogenicity: loss of homogenous texture to be replaced by speckled coarse texture.
  - Irregular liver margins.
  - Attenuation of intra-hepatic portal and hepatic veins.
- ***Presence of periportal thickening.***
- ***Portal vein diameter.***
- ***Splenic size:*** The size was classified according to the longest axis which was measured from upper to lower pole. Normally, it is up to 12-13 cm. If enlarged, it was classified as mild (13-16), moderate (16-20), or huge (> 20 cm) splenomegaly [10, 11]***.***
- ***Presence of porto-systemic collaterals.***
- ***The presence of ascites*** [12]***.***
- ***Criteria suggestive of portal hypertension by ultrasonography:*** Portal vein diameter more than 13 mm and loss of variation in diameter during respiration. The presence of portosystemic collaterals, splenomegaly and ascites [9]***.***

**VIII- Upper Gastrointestinal Endoscopy:**

- This was performed using the **(Pentax EPM 3500)** endoscopy. To evaluate the presence and grades of varices in addition to any relevant upper GIT lesions.
- Esophageal varices (EV) were classified according to ***Westaby et al.*** [13] into:
  - Grade I: Varix is in flush with the wall of the esophagus.
  - Grade II: Prortusion of the varix but not more than half way to the center of the lumen.
  - Grade III: Prortusion of the varix more than half way to the center of the lumen.
  - Grade IV: The varices are so large that they meet at the midline.
- Also, patients were classified into two groups [14, 15]:
  - Small varices: included grades (I, I-II, II).
  - Large varices: included grades (II-III, III, III-IV, IV).
- Gastric varices (GV) were classified into two types [16]:
  - Gastroesophageal varices: when GV were associated with EV.
  - Isolated gastric varices (IGV) occur in the absence of EV.
- Red color signs: were classified as follows [17]:

a. Red Wale Markings "RWM": longitudinal dilated venules which resemble those of a wale of whip marks.

b. Cherry Red Spot "CRS": small red spots, usually multiple and about 2 mm or less in diameter.

c. Hematocystic Spots "HCS": a large and solitary red spot which is usually found on tortuous varices.

- Portal Hypertensive Gastropathy (PHG):

It was classified according to ***(Baveno III consensus classification)*** [18] into:

Mild PHG: mild mosaic like pattern (uniform polygonal area surrounded by whitish yellow depressed borders).

Severe PHG: when mosaic pattern is superimposed by any red signs (red point lesions, cherry red spots, and black brown spot).

- **Statistical methodology:**

Data collected on a precoded pro-forma were subjected to revision and introduction to a Personal Computer (PC) where data management was conducted using Statistical Package for Social Sciences (SPSS) software computer program version (12.0).

Statistical presentation and analysis of the present study was conducted using the mean, standard error, unpaired student t-test, linear correlation coefficient, Student t-test [Unpaired], chi-square test and
ROC curve.

**Sensitivity: -** Probability that the test results will be positive when the disease is present (true positive rate, expressed as a percentage).

**Specificity: -** Probability that the test results will be negative when the disease is not present (true negative rate, expressed as a percentage).

**Positive Predictive value (PPV):** - (probability that the disease is present when the test is positive).

**Negative Predictive value (NPV):** - (probability that the disease is present when the test is negative).

**Accuracy: -** The ratio of the true positive and true negative in all patients.

**Results:**

**I) Description of the sample; characteristics of the study group (n=33):**

Twenty patients were males (60.61%) and thirteen patients were females (39.39%). The ages of the studied patients ranged between 37-67 years (mean age 52.94 ± 7.91 years).

Regarding clinical data of the studied patients, general examination revealed that all patients except one had bilateral lower limb edema (96.97%). Pallor, flapping tremors and jaundice were the most common signs.

Abdominal examination revealed splenomegaly in 31 cases (93.94%) and hepatomegaly in 22 cases (66.67%).

Twenty patients had moderate ascites (60.61%) and thirteen patients had tense ascites (39.39%).

Regarding the hepatitis markers of the studied patients, HCVAb was positive in 31 cases (93.94%). Both HCVAb and HBsAg were positive in one case (3.03%), both HCVAb and HBsAg were negative in one case (3.03%) who was diagnosed as Budd-Chiari Syndrome.

Regarding Child Pugh Classification of the studied patients, 29 patients (87.88%) were Child class B and four patients (12.12%) were Child class C.

Regarding the physical analysis of the ascitic fluid, the colour was yellow in 30 patients (90.91%) and red in three patients (9.09%), the aspect was clear in 20 patients (60.61%) and turbid in 13 patients (39.39%) and the reaction was alkaline in all patients (100%).

Regarding the chemical analysis of the ascitic fluid, the ascitic fluid albumin ranged between 0.2 - 3.3 (mean albumin 1.37 ± 0.70) gm/dl, ascitic fluid total protein ranged between 1.2 - 4.9 (mean total protein 2.14 ± 0.68) gm/dl, LDH in ascitic fluid ranged between 63 - 538 (mean LDH 139.88 ± 89.64) gm/dl and glucose ranged between 64 - 346 (mean glucose 148.39 ± 69.55) gm/dl.

Regarding the bacteriological analysis of the ascitic fluid, gram stain showed occasional cells (mainly lymphocytes) in all the ascitic fluid samples, Ziel Nielsen stain and leishmann stain were negative in all samples. Cultures of all samples were negative for bacteria after inoculation for 48 hours. Cell count ranged between 6-1280 cells/HPF (mean cell count 85.55 ± 219.26). Only one patient was evident to have spontaneous bacterial peritonitis.

Regarding the cytological analysis of the ascitic fluid, no malignant cells could be detected in any sample.

Serum ascites albumin gradient (SAAG) was calculated in all the studied patients and it ranged between 0.4 – 2.6 (mean SAAG 1.27 ± 1.27) gm/dl.

Abdominal ultrasound revealed that the liver size was average (11-15 cm) in 24 patients (72.73%), enlarged (>15 cm) in eight patients (24.24%) and shrunken (<11 cm) in one patient (3.03%). The mean liver size was 14.6 ± 1.17 cm.

Twenty two patients (66.67%) had coarse liver, nine patients (27.27%) had bright coarse liver and two patients had bright liver (6.06%). There was periportal thickening in 7 cases (21.21%). The mean portal vein diameter in the studied patients was 14.79 ± 2.05 mm.

Regarding the ultrasonographic findings of the spleen, 21 patients (63.64%) had mildly enlarged spleen (13-16 cm), 11 patients (33.33%) had moderately enlarged spleen (16-20 cm) and one patient (3.03%) had hugely enlarged spleen (>20 cm). The mean size of the spleen in the studied patients was 15.90 ± 1.40 cm.

Portosystemic collaterals were detected in four patients (12.12%).

The amount of ascites was moderate to severe in all the studied patients.

Upper GIT endoscopy revealed varices in 28 patients (84.85%) and no varices in five patients (15.15%).

Among those with varices, 20/28 patients (71.43%) had isolated EV and 8/28 patients (28.75%) had EV with gastric extension (gastroesophageal varices).

Five cases (17.86%) had grade I, three cases (10.71%) had grade I- II, five cases (17.86%) had grade

II, ten cases (35.71%) had grade II-III, three cases (10.71%) had grade III and two cases (7.14%) had grade III-IV EV.

Among those with varices, only 4 cases (14.29%) had cherry red spots. No other risky signs were detected.

Regarding the presence of portal hypertensive gastropathy (PHG) among the investigated patients, 25 patients (75.76%) had PHG while the remaining 8 patients (24.24%) showed no evidence of PHG.

Among patients with portal hypertensive gastropathy (PHG), 19 patients (76%) had severe PHG and 6 patients (24%) had mild PHG.

**II) Statistical Analysis:**

A) According to the SAAG values, patients were divided into two groups:

- ***High SAAG:*** 27 Patients (81.82%) were with high SAAG (≥1.1 g/dl).
- ***Low SAAG***: 6 patients (18.18%) were with low SAAG (<1.1 g/dl).

Upper GIT endoscopy revealed varices in 22 patients (81.5%) in high SAAG group and all patients (100%) in low SAAG group with non significant statistical difference as shown in **Table (1).**

Among the 22 patients with varices in the high SAAG group, 16 patients (72.72%) had isolated EV and 6 patients (27.27%) had EV with gastric extension (gastroesophageal varices).

Among the six patients with varices in the low SAAG group, four patients (66.67%) had isolated EV and two patients (33.33%) had EV with gastric extension (gastroesophageal varices).

**Table (2)** shows that there is no significant statistical difference between SAAG groups regarding grading of EV.

Comparison between patients with varices and those without as regard the SAAG of ascitic fluid of the studied patients shows no significant statistical difference as shown in **Table (3).**

Comparison between patients with small varices and those with large varices as regard total protein, serum albumin, ascitic albumin and SAAG shows no significant statistical difference, **Table (4).**

Comparison between patients with different grades of varices as regard total protein, serum albumin, ascitic albumin and SAAG showed non significant statistical difference **(Table 5).**

**Table (6)** shows no significance statistical relation between SAAG groups and the size of varices.

**Patients' distribution according to the grade of esophageal varices and the degree of SAAG:**

The grade of the EV in patients with High SAAG, according to the degree of SAAG was as follows:

In SAAG between 1.10 and 1.49 g/dl, four patients (14.29%) had grade I EV, two patients (7.14%) had grade I-II EV, 5 patients (17.86%) had grade II EV, 8 patients (28.57%) had grade II- III EV, 2 patients (7.14%) had grade III EV and 2 patients (7.14%) had grade III-IV EV.

In SAAG between 1.50 and 1.99 g/dl, only one patient (3.57%) had grade I-II EV and one patient (3.57%) had grade III EV.

In SAAG ≥ 2.0 g/dl, only one patient (3.57%) had grade I EV and two patients (7.14%) had grade II-III EV.

The grade of the EV did not demonstrate significant statistical association and showed no correlation with the degree of SAAG as shown in **Table (7).**

**III) Diagnostic validity test (Receiver Operating Characteristic curve):**

**Figure (1)** shows the Receiver Operating Characteristic (ROC) curve displaying discrimination between presence and absence of varices. The Area under the curve (AVC) is (0.561). This denotes fair discrimination between them.

**Table (8) and Figure (2)** show the sensitivity, specificity, positive predictive value **(PPV)** and negative predictive value (**NPV**) at cutoff (> 1.4) of SAAG for the presence of varices:

A cutoff ">1.4" for SAAG to predict the presence of varices yielded a specificity and a positive predictive value of 100% (meaning low false positive rate), the accuracy of this cutoff was 56.1%. However, it had a low sensitivity and a low negative predictive value (meaning high false negative rate).

**Figure (3)** shows the Receiver Operating Characteristic (ROC) curve displaying discrimination between small and large varices. The Area under the curve (AUC) is **(0.600)**. This denotes fair discrimination between them.

**Table (9) and Figure (4)** show the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at cutoff (> 1.2) of SAAG for discrimination between small and large varices:

A cutoff ">1.2" for SAAG to discriminate between large and small varices yielded a specificity of 69.2% and a positive predictive value of 66.7%, the accuracy of this cutoff was 60%. However, it had a relatively low sensitivity and low negative predictive value (meaning relatively high false negative rate).

**Table (1): Comparison between high SAAG group and low SAAG group regarding presence of varices among the investigated patients (n=33).**

| | High SAAG (n=27) | | Low SAAG (n=6) | | P-value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Varices | 22 | 81.5% | 6 | 100% | 0.252 |
| No varices | 5 | 18.5% | 0 | 0.0% | |

**Table (2): Comparison between SAAG groups regarding grading of esophageal varices (Among patients with varices, n=28):**

| | High SAAG with Varices (n=22) | | Low SAAG with Varices (n=6) | |
|---|---|---|---|---|
| | N | % | N | % |
| I | 5 | 22.73 | 0 | 0.00 |
| I-II | 2 | 9.09 | 1 | 16.67 |
| II | 3 | 13.64 | 2 | 33.33 |
| II-III | 8 | 36.36 | 2 | 33.33 |
| III | 2 | 9.09 | 1 | 16.67 |
| III-IV | 2 | 9.09 | 0 | 0.00 |
| **Chi-square ($X^2$)** | **2.526** | | | |
| **P- value** | **0.866** | | | |

**Table (3): Comparison between patients with varices and those without as regard the SAAG of ascitic fluid of the studied patients (n=33):**

| | No varices (n=5) | | | Varices (n=28) | | | P-value |
|---|---|---|---|---|---|---|---|
| | Mean | ± | SD | Mean | ± | SD | |
| Total protein | 2.60 | ± | 1.33 | 2.03 | ± | 0.49 | 0.083 |
| Serum Albumin | 3.08 | ± | 0.75 | 2.53 | ± | 0.46 | 0.032 |
| Ascitic Albumin | 1.72 | ± | 1.03 | 1.31 | ± | 0.63 | 0.231 |
| SAAG | 1.16 | ± | 0.20 | 1.29 | ± | 0.53 | 0.598 |

**Table (4): Comparison between patients with small varices and those with large varices as regard total protein, serum albumin, ascitic albumin and SAAG of the studied patients (n=28):**

| | Small varices (n=13) | | | Large varices (n=15) | | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | ± | SD | Mean | ± | SD | T | P-value |
| Ascitic total protein | 1.915 | ± | 0.285 | 2.127 | ± | 0.602 | -1.156 | 0.258 |
| Serum albumin | 2.492 | ± | 0.484 | 2.560 | ± | 0.450 | -0.383 | 0.705 |
| Ascitic albumin | 1.292 | ± | 0.612 | 1.320 | ± | 0.667 | -0.114 | 0.910 |
| SAAG | 1.192 | ± | 0.461 | 1.373 | ± | 0.587 | -0.897 | 0.378 |

**Table (5): Comparison between patients with different grades of varices as regard total protein, serum albumin, ascitic albumin and SAAG of the studied patients (n=28):**

| | Total protein | | | Serum albumin | | | Ascitic albumin | | | SAAG | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | ± | SD | Mean | ± | SD | Mean | ± | SD | Mean | ± | SD |
| I | 6.760 | ± | 0.518 | 2.620 | ± | 0.589 | 1.240 | ± | 0.792 | 1.380 | ± | 0.466 |
| I-II | 5.840 | ± | 2.137 | 2.433 | ± | 0.611 | 1.267 | ± | 0.929 | 1.133 | ± | 0.702 |
| II | 6.833 | ± | 0.115 | 2.400 | ± | 0.367 | 1.360 | ± | 0.230 | 1.040 | ± | 0.313 |
| II-III | 6.180 | ± | 0.801 | 2.570 | ± | 0.427 | 1.330 | ± | 0.757 | 1.340 | ± | 0.506 |
| III | 6.550 | ± | 0.718 | 2.233 | ± | 0.493 | 1.133 | ± | 0.635 | 1.100 | ± | 0.624 |
| III-IV | 6.733 | ± | 1.361 | 3.000 | ± | 0.000 | 1.550 | ± | 0.212 | 1.950 | ± | 0.919 |
| R | 0.087 | | | -0.221 | | | -0.125 | | | 0.163 | | |
| P-Value | 0.630 | | | 0.217 | | | 0.487 | | | 0.365 | | |

**Table (6): Relation between SAAG groups and size of varices (Among patients with varices, n=28):**

| | | | High SAAG with Varices (n=22) | Low SAAG with Varices (n=6) |
|---|---|---|---|---|
| Size of varices | Small | N | 10 | 3 |
| | | % | 45.45 | 50.00 |
| | Large | N | 12 | 3 |
| | | % | 54.55 | 50.00 |
| Chi-square ($X^2$) | | | 0.101 | |
| P-value | | | 0.750 | |

**Table (7): Patient's distribution according to the grades of EV and the degree of SAAG:**

| Grades of EV | SAAG Value (g/dl) No. of patients (%) | | | |
|---|---|---|---|---|
| | 1.1 – 1.49 | 1.50 – 1.99 | ≥ 2 | Total |
| | N (%) | N (%) | N (%) | N (%) |
| I | 4 (14.29) | 0(0.00) | 1 (3.57) | 5 (17.86) |
| I-II | 2 (7.14) | 1 (3.57) | 0 (0.00) | 3 (10.71) |
| II | 5 (17.86) | 0 (0.00) | 0 (0.00) | 5 (17.86) |
| II-III | 8 (28.57) | 0 (0.00) | 2( 7.14) | 10 (35.71) |
| III | 2 (7.14) | 1 (3.57) | 0 (0.00) | 3 (10.71) |
| III-IV | 2 (7.14) | 0 (0.00) | 0 (0.00) | 2 (7.14) |
| Chi-square ($X^2$) | 10.388 | | | |
| P-value | 0.407 | | | |

Percentages are calculated among patients with varices (n=28).

**Table (8): The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at cutoff ">1.4" of SAAG for the presence of varices:**

| Cutoff | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|
| > 1.4 | 21.4 | 100.0 | 100 | 18.5 | 0.561 |

**Table (9): The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at cutoff ">1.2" of SAAG for discrimination between small and large varices:**

| Cutoff | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|
| > 1.2 | 53.3 | 69.2 | 66.7 | 56.2 | 0.600 |

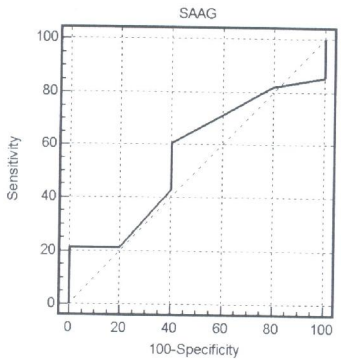


**Figure (1):** Receiver Operating Characteristic (ROC) curve displaying discrimination between presence and absence of varices. Area under the curve (AVC) is (0.561).

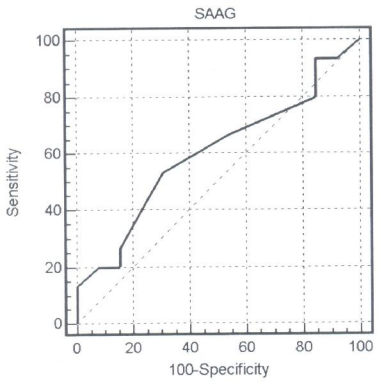


**Figure (2):** The sensitivity, specificity, PPV and NPV at cutoff "> 1.4" of SAAG for the presence of varices.

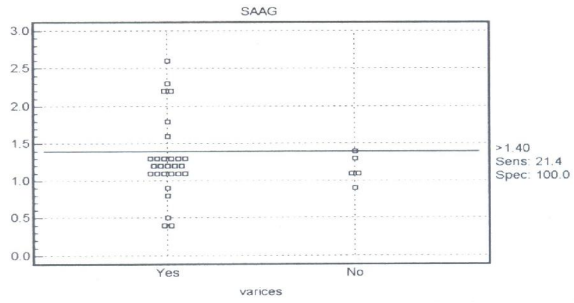


**Figure (3)** The Receiver Operating Characteristic (ROC) curve displaying discrimination between small and large varices. The Area under the curve (AUC) is (0.600).

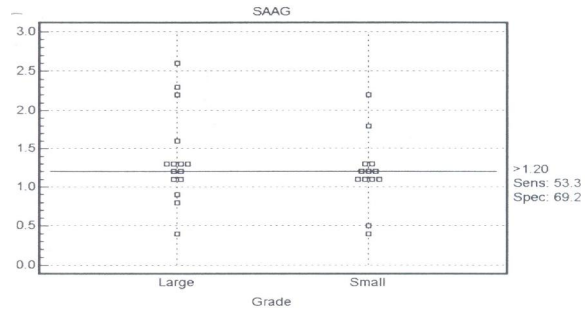


**Figure (4):** The sensitivity, specificity, PPV and NPV at cutoff ">1.2" of SAAG for discrimination between small and large varices.

## Discussion

Serum-ascites albumin gradient had been considered as the most valuable parameter to discriminate patients with malignancy-related ascites from those without. SAAG is superior to previously proposed transudate-exudate concept, not only because of its higher diagnostic accuracy but also because it provides a better approach to pathogenesis of ascitic fluid accumulation [19, 20].

The term transudative-exudative ascites should be replaced with the ascites related to portal hypertension (high gradient) and ascites not related to portal hypertension (low gradient) respectively [19, 21].

The SAAG is able to define the presence or absence of portal hypertension with an accuracy of 96.7% [22]. This was confirmed by ***Beg et al.*** [19] who observed that the serum-ascites albumin gradient (SAAG) had a diagnostic sensitivity of 94.73% and 96% accuracy compared to ascitic fluid total protein (AFTP), which was 65.62% and 68% respectively. Although, the level of AFTP, apart from the exudate-transudate concept, has some value for certain cases (a low level of AFTP implicates a high risk of spontaneous bacterial peritonitis) [23].

SAAG was proved to be an accurate test despite ascitic fluid infection, diuresis, therapeutic paracentesis, albumin infusion, and etiology of liver disease [24].

***Akriviadis et al.*** [25] observed that the diagnostic accuracy was 98% for the serum/ascites albumin gradient. In patients with infected ascites, diagnostic accuracy was 89%. They concluded that the serum/ascites albumin gradient is a reliable marker distinguishing ascites related to portal hypertension from all other causes of ascitic fluid collection, regardless of the presence of bacterial infection.

However, SAAG sensitivity of detecting a gradient less than 1.1 g/dl was reported to be low (62%) in the large prospective study conducted by ***Albillos et al.*** [26]. Similarly, ***Chen et al.*** [27] reported that, although SAAG offered the best diagnostic accuracy (90.2%) and specificity (98.9%), its sensitivity (62.1%) was not good enough.

In several studies on cirrhosis due to alcohol, the correlation between SAAG and esophageal varices was emphasized and additionally, SAAG was proposed to be a factor determining the degree of portal hypertension and the prognosis of patients in cirrhosis due to alcohol [28].

There are scanty studies which evaluated the relation between SAAG and EV in patients with non-alcoholic cirrhosis [29].The current study aimed to investigate the correlation between SAAG and presence of esophageal varices (EV) and their grades in patients with portal hypertension due to chronic liver disease.

Calculation of SAAG was done by subtracting the albumin concentration of the ascitic fluid from the albumin concentration of a serum specimen obtained on the same day, (serum albumin - ascitic fluid albumin) [6]. Patients were classified according to SAAG level, high SAAG was considered to be present when the SAAG was $\geq$ 1.1 g/dl and low SAAG when it measured < 1.1 g/dl [5].

In the current study, 27 patients (81.82%) had high SAAG and 6 patients (18.18%) had low SAAG. Also, ***Gurubacharya et al.*** [6] found that 25 of 32 (78.13%) patients had high SAAG and 7 of 32 (21.87%) had low SAAG. Similarly, SAAG was found to be >1.1 in 96.5% of the studied patients by ***Al-Knawy,*** [21] and <1.1 in the remaining 3.5%.

Although the present study was conducted on patients with portal hypertension due to chronic liver disease, we observed that 6 patients (18.18%) had low SAAG (<1.1 g/dl).

The discrepancy in the results of SAAG level and its relation to portal hypertension may be attributed

to two factors; first, the 3.3% error in its diagnostic accuracy due to the very narrow range of the level of ascitic fluid albumin concentration (0 to 1 g/dl in some cases) [24]. Second, the discrepancy in the results of SAAG level may be caused by usual methods of estimation of albumin concentration (dye binding and shift in color when a dye is bound by albumin) [30, 31]. More appropriate methods for determination of albumin concentration in body fluids in which albumin concentration is normally low (i.e., urine and CSF), includes several formats of electrophoresis, radioimmunoassays (RIA) and immunoassays [32]. They need special equipments, which may not be available in ordinary clinical laboratories, particularly in developing countries [33].

Another potential problem with SAAG occurs when the serum and ascitic fluid specimens are not obtained simultaneously. This is because both serum and ascitic fluid albumin change over time in parallel, so that the difference between them is stable [24]. However, in the present study this problem was overcomed by obtaining specimens to measure albumin from serum and ascites on the same day.

In the current study, patients with low SAAG were revaluated. There was no history or clinical findings suggestive for TB or malignancy. Laboratory data as regards the liver enzymes, liver function tests and viral markers confirmed the etiology of chronic liver disease. Also, ultrasonographic findings of those patients were fullfling the criteria suggestive of portal hypertension.

The presence of some sonographic criteria, namely matted intestinal loops, intrapretioneal adhesions, abdominal lymphadenopathy and extrahepatic masses were reported to be highly specific in detection of exudative ascites but with a low sensitivity [34]. These findings could not be detected in patients of low SAAG in the present study.

SAAG was helpful in classifying 100% of transudative ascites rather than 67% on the basis of ascitic fluid protein, [35], but the latter remains a useful adjunct in the differential diagnosis of ascites [22]. Ascitic fluid analysis of patients in the current study revealed that the mean ascitic fluid total protein was 2.14 ± 0.68 mg/dl (transudate).

***Khan*** [36] found that during the initial evaluation of patients with low gradient ascites, ascitic fluid glucose and LDH levels are useful indicators for separating tuberculous from malignant ascites. Consequently, low LDH and glucose levels indicate TB, while high levels suggest cancer as the major cause [36, 37]. Glucose and LDH of low SAAG patients in the current study showed no changes suggestive of TB or malignancy.

A low SAAG does not differentiate between tuberculous and malignant ascites. Consequently, there is still need to test for cytology or culture for mycobacteria [23]. Ziel Nielsen stain and cultures of ascitic fluid for TB in the current study were negative. In the study conducted by ***Khan et al.*** [38], cytological evaluation of ascitic fluid was helpful in the detection of malignant ascites; it was positive in 75% of patients. Cytological evaluation in the current study showed no malignant cells.

The results of the present study were supported by many studies which were conducted to evaluate the correlation between SAAG and EV in patients with nonalcoholic cirrhosis. A SAAG <1.1 was found by ***Kajani et al.*** [28] in three out of fourteen non alcoholics with cirrhosis in the absence of an abdominal malignancy. They concluded that SAAG <1.1 is not diagnostic of abdominal malignancy but can occur in those with advanced non malignant hepatic disease.

***Das et al.*** [39] studied the comparative utility of SAAG and ascitic fluid total protein for differential diagnosis of ascites. They found that the SAAG was > 1.1 in 85% cases of CLD patients with presumed portal hypertension. On the other hand, SAAG < 1.1 would suggest absence of significant portal hypertension in ascitic patients. They emphasized that SAAG did not provide the exact cause of ascites despite its superior discriminatory power. The presence of a high albumin gradient did not diagnose cirrhosis. It simply indicated the presence of portal hypertension. Similarly, a low albumin gradient did not diagnose any specific condition.

In a study done by ***Al-Knawy,*** [21] EV were found in all the studied 87 patients with non-alcoholic cirrhosis; SAAG was found to be >1.1 in 82 of these patients and <1.1 in the remaining five, who were due to viral causes of liver cirrhosis and had no superimposed spontaneous bacterial peritonitis or hepatocellular carcinoma.

In the current study, upper GIT endoscopy revealed varices in 22 patients (81.5%) in high SAAG group and all patients (100%) in low SAAG group with no significant statistical difference. Likewise, ***Abdel Hakam*** [40] concluded that no significant difference was found between patients with varices and those without regarding the SAAG level.

On the contrary, ***Torres et al.*** [5] found that esophageal varices were present in 17 of 25 (68%) patients with high SAAG and in none of six (0%) patients with low SAAG ($p = 0.028$) and in patients with nonalcoholic liver disease, only three of 11 (27.3%) had EV ($p < 0.05$). Also, endoscopic examination by ***Abo Hamila*** [41] revealed that 20 patients with high SAAG value had esophageal varices, on the other hand all 6 patients with low SAAG value had no varices. In contrast to the results of the present study, ***Gurubacharya et al.*** [6] found that esophageal varices were present in 18 of 25 (72%) patients with High SAAG and in none of 7 (0%) patients with Low

SAAG (p =<0.001).

Also, ***Masroor et al.*** [42] studied 50 patients with liver cirrhosis. SAAG was found to be between 1.1 and 3.2 in all 50 patients while esophageal varices were present in 46 (92%) of them. The grade of the EV in patients with High SAAG, according to the degree of SAAG was as follows:

In SAAG between 1.10 and 1.49 g/dl, four patients (14.29%) had grade I EV, two patients (7.14%) had grade I-II EV, 5 patients (17.86%) had grade II EV, 8 patients (28.57%) had grade II- III EV, 2 patients (7.14%) had grade III EV and 2 patients (7.14%) had grade III-IV EV.

In SAAG between 1.50 and 1.99 g/dl, only one patient (3.57%) had grade I-II EV and one patient (3.57%) had grade III EV. In SAAG ≥ 2.0 g/dl, only one patient (3.57%) had grade I EV and two patients (7.14%) had grade II- III EV. The grade of the EV did not demonstrate significant statistical association and showed no correlation with the degree of SAAG. These results were similar to all previous studies in this aspect.

***Torres et al.*** [5] found that among patients with high SAAG, EV were present in four of 10 (40%) with SAAG values of 1.10 - 1.49 g/dl; in four of 6 (66.7%) with SAAG values of 1.50 -1.99 g/dl; and in nine of nine (100%) with SAAG values of >2.0 g/dl (p = 0.049). Thus, in their study, the size of the EV in patients with ascites and high SAAG was not associated with the degree of SAAG.

***Demirel et al.*** [29] also classified the patients by their SAAG values; two of four patients with SAAG values between 1.1 and 1.49 had esophageal varices, as did 13 of 15 patients with SAAG values between 1.5 and 1.99, and all of the patients with SAAG values greater than 2.0.

In the study of ***Gurubacharya et al.*** [6], EV were present in four of 8 patients (50%) with SAAG values of 1.10 - 1.49 g/dl; four of seven patients (57.1%) with SAAG values of 1.50-1.99 g/dl; and in ten of ten (100%) with SAAG values of ≥ 2.0 g/dl (p = 0.037). They concluded that the size of EV had no association with the level of SAAG in patients with High SAAG (p = 0.426).

***Abo Hamila*** [41] graded esophageal varices in patients with high SAAG as follows: In SAAG values between 1.10 - 1.49 g/dl, one patient (20%) had grade I EV, two patients (40%) had grade II EV and two patients (40%) had grade III EV. In SAAG values between 1.50 - 1.99 g/dl, two patients (40%) had grade I EV, two patients (40%) had grade II EV and one patient (20%) had grade III EV. In SAAG values of ≥ 2.0 g/dl, one patient (10%) had grade I EV, two patients (20%) had grade II EV, four patients (40%) had grade III EV and three patients (30%) had grade IV EV. They found no significant relation between the degree of SAAG and the grading of EV (p: 0.736).

Comparisons between patients with varices and those without varices, patients with small varices and those with large varices and between different grades of varices as regards ascitic total protein, ascitic albumin and SAAG level showed no significant statistical difference.

This comes in agreement with the study of ***Abdel Hakam*** [40] which revealed no significant difference between patients with large varices and those with small varices regarding the SAAG level.

However, this was in contrast to the study of ***Masroor et al.*** [42] who found that the presence and size of EV was directly correlated with the degree of SAAG.

There was also no significant correlation between grades of esophageal varices and serum albumin, ascitic albumin, ascitic total protein or SAAG level in the current study. These is partially consistent with ***Demirel et al.*** [29] who found no correlation between the degree of the esophageal varices and serum levels of albumin (p-0.7) and SAAG (p-0.2); but a weak correlation was found between the degree of the esophageal varices and ascitic fluid albumin (p=0.03, r-0.30). The correlation that has been previously found to exist between SAAG and esophageal varices could not be found in their patients with non-alcoholic cirrhosis.

In the contrary, ***Kajani et al.*** [28] found a weak correlation between SAAG and the degree of EV (r=0.02).

In the current study, Receiver Operating Characteristic (ROC) curve was displayed in order to discriminate between presence and absence of varices.

A cutoff ">1.4" for SAAG to predict the presence of varices yielded a specificity and a positive predictive value of 100% (meaning low false positive rate), the accuracy of this cutoff was 56.1%. However, it had a low sensitivity and a low negative predictive value (meaning high false negative rate).

This was concordant to ***Torres et al.*** [5] who found that a SAAG value of > 1.435 ± 0.015 g/dl is a useful means to predict the presence of EV in patients with ascites (cutoff point for the highest predictive value: positive = 87.5% and negative = 66.7%).

A higher cutoff was obtained by ***Demirel et al.*** [29] and ***Gurubacharya et al.*** [6] who found that all of the studied patients with SAAG value greater than 2.0 had esophageal varices.

In the current study, a cutoff ">1.2" for SAAG to discriminate between large and small varices yielded a specificity of 69.2% and a positive predictive value of 66.7%, the accuracy of this cutoff was 60%. However, it had a relatively low sensitivity and low negative predictive value (meaning relatively high false negative rate).

This was comparable with the results of ***Shalaby*** [43] who found that SAAG level of more than 2.2 g/dl, was a powerful indicator that the patient had large varices with high risk to bleed.

**Conclusion:** A cutoff ">1.4" for SAAG to predict the presence of varices yielded a specificity and a positive predictive value of 100%, the accuracy of this cutoff was 56.1%.

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